REMARKS

Claims 70-72, 75, 77, 79-83, 87-89 and 93-98 are pending and under examination. Claims 70-72 have been canceled. New claims 99-124 have been added. Support for the new claims can be found throughout the specification and the claims as filed. In particular, support can be found, for example, in original claims 8-11 and 69-72, and on page 12, lines 8-26, and page 50, lines 20-23 and 28-32. Accordingly, these new claims do not raise an issue of new matter and entry thereof is respectfully requested.

Applicants appreciate the indication by the Examiner that claim 72 would be allowable if rewritten in independent form. New claim 103 corresponds to claim 72 rewritten in independent form. New claims 104-124 depend from new claim 103. New claims 104 and 105 correspond to previous claims 70 and 71, which have been canceled. New claims 106-124 parallel claims 77, 79-83, 87-89 and 93-98, respectively.

Rejection Under 35 U.S.C. § 112, First Paragraph

The rejection of claims 70, 71, 82, 88, 94 and 97 under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description is respectfully traversed. Applicants respectfully submit that the specification provides sufficient description and guidance for the claimed isolated anti-TPBD antibodies.

With respect to claims 70 and 71, which have now been rewritten as new claims 104 and 105, respectively, the Office Action asserts that the specific limitations of claims 70 and 71 were not recited as part of the antibody modulating activities in the specification (for example, on page 52, lines 15-31) or the claims as filed. First, Applicants respectfully point out that the limitations of claims 70 and 71 were specifically recited in original claims 70 and 71. Claims 70 and 71 (new claims 104 and 105) have only been amended to have antecedent basis from the base claim and to change the dependency. Therefore, the limitations of claims 70 and 71 (new claims 104 and 105) are clearly provided in the originally filed claims.

Second, it is respectfully submitted that the specification additionally supports claims 70 and 71 (new claims 104 and 105). The specification teaches that invention anti-TPBD antibodies can be used to modulate the activity of a TPBD polypeptide (page 52, lines 15-31). The specification

further teaches that the term "modulate" refers to a compound's ability to increase, decrease or otherwise modify the biological activity of an invention TPBD protein, such as TNFR family-binding, TRAF protein binding activity, and TRAF-associated protein binding activity (page 52, lines 19-26). Previous claim 72 (new claim 103), from which claims 70 and 71 (new claims 104 and 105) depend, recites that the claimed antibody inhibits the association of the TPBD with a TNF family receptor, TRAF protein or a TRAF-associated protein, that is, exemplary biological activities of TPBD protein (page 52, lines 24-26). Claim 70 (new claim 104) recites the TNF family receptor TNF-R2, the TRAF protein human TRAF6, and the TRAF-associated protein I-TRAF. Claim 71 (new claim 105) recites the TNF family receptor CD40, the TRAF protein human TRAF2, and the TRAF-associated protein I-TRAF. Thus, claims 70 and 71 (new claims 104 and 105) merely recite specific TNF family receptors, TRAF proteins and TRAF-associated proteins. Accordingly, Applicants respectfully submit that the specification and originally filed claims provide sufficient description and guidance for claims 70 and 71 (new claims 104 and 105). Therefore, Applicants respectfully request that this rejection be withdrawn.

Regarding claims 82, 88, 94 and 97, the Office Action asserts that the specification as filed contemplates only hybridomas as the cell line producing the claimed monoclonal antibody (referring to page 51, line 10), whereas the claims encompass prokaryote and eukaryote cell lines that recombinantly produce the claimed antibodies, which are asserted to be larger than the scope of a hybridoma cell line. In contrast to the assertion in the Office Action, the specification teaches that antibodies can be produced by hybridoma, chemical synthesis or recombinant methods (page 51, lines 9-10). Accordingly, Applicants respectfully submit that the specification provides sufficient description and guidance for the claimed cell lines producing monoclonal antibodies, as recited in claims 82, 88, 94 and 97. Therefore, Applicants respectfully request that this rejection be withdrawn.

Rejections Under 35 U.S.C. § 103

The rejection of claims 75, 77, 80, 81, 83, 87, 89, 96 and 98 under 35 U.S.C. § 103 as allegedly obvious over Comb et al., U.S. Patent No. 6,441,140, in view of Brodeur et al., J. Biol. Chem. 272:19777-19784 (1997), is respectfully traversed. Applicants respectfully submit that the claims are unobvious over Comb et al., alone or in combination with Brodeur et al.

Applicants respectfully submit that there would have been no motivation to combine the teachings of Comb et al. with Brodeur et al. to obtain the claimed antibodies. The Office Action acknowledges that Comb et al. does not teach or suggest antibodies that bind to the claimed SEQ ID NOS:12 or 25. However, the Office Action asserts that it would have been obvious to make monoclonal and polyclonal antibodies to the PXQX(T/S) motif described in Brodeur et al. The Office Action asserts that Brodeur et al. teaches that the motif PXQX(T/S) is a TRAF recognition site, referring to page 19782, column 1, lines 2-6. However, Brodeur et al. teaches that analysis of the deleted sequences of constructs revealed that "the distal COOH terminus of LMP-1 contained the putative TRAF recognition site designated LMP-1 C in Fig. 1A based on the presence of the PXQX(T/S) motif originally found in the CD40 receptor motif" (page 19792, left column, first paragraph; emphasis added). Thus, Brodeur et al. teaches that this is a "putative" TRAF recognition site. Brodeur et al. further discloses that the C140 and C35 constructs (both of which contain sequences that include the C-terminus of LMP-1 containing the PXQX(T/S) motif) were tested for their ability to bind TRAF2, TRAF3, TRAF5 and TRAF6, and they "consistently failed to observe an interaction that could be mediated through the LMP-1 C site. This site may therefore represent a binding region important for interaction with as yet uncharacterized TRAF molecules, or the presence of the motif may be fortuitous" (page 19782, left column, first paragraph; emphasis added). Thus, in contrast to the assertion in the Office Action, Brodeur et al., at best, describes the PXQX(T/S) motif as a putative TRAF recognition site for which they failed to show any TRAF recognition activity. Furthermore, Brodeur et al. provides no teaching or suggestion for making an antibody to the "fortuitous" motif. Clearly, absent the teaching in Applicants' specification, one skilled in the art would have had no motivation to combine the teaching of Comb et al. with that of Brodeur et al. to achieve Applicants' claimed antibodies. Absent such a motivation, Applicants respectfully submit that a *prima facie* case of obviousness has not been established.

Applicants respectfully submit that the claimed antibodies are unobvious over Comb et al., alone or in combination with Brodeur et al. Accordingly, Applicants respectfully request that this rejection be withdrawn.

The rejection of claims 75, 79, 81 and 93 under 35 U.S.C. § 103 as allegedly obvious over Nagai et al., FEBS Lett. 418:23-26 (1997), and Campbell, Monoclonal Antibody Technology pp. 1-32, Elsevier Science Publishers, Amsterdam (1985), is respectfully traversed. Applicants

respectfully submit that the claims are unobvious over Nagai et al., alone or in combination with Campbell.

Claim 75 is directed to an isolated anti-TPBD antibody having specific reactivity with a TPBD amino acid sequence selected from the group consisting of SEQ ID NOS: 12, 24 and 25, and Nagai et al. is asserted in the Office Action to teach an amino acid sequence, SPOP, "consisting of all of residues 1-132 of SEQ ID NO:24." The Office Action acknowledges that Nagai et al. does not teach an antibody that binds the SPOP protein without an HA tag but asserts that it would have been obvious to make monoclonal antibodies based on the teaching in Campbell.

Applicants respectfully disagree with the assertion that Nagai et al. teaches a sequence "consisting of all residues 1-132 of SEQ ID NO:24" (emphasis added). To the contrary, Nagai et al. describes an SPOP protein having 374 amino acids (see abstract and Figure 2A), not a peptide consisting of the 132 amino acids of SEQ ID NO:24. Thus, Nagai et al. does not teach or suggest the specifically recited sequence referenced as SEQ ID NO:24. Accordingly, Nagai et al., alone or in combination with Campbell, does not teach every element of the claimed antibodies. Absent such a teaching or suggestion, Nagai et al., alone or in combination with Campbell, cannot render the claimed antibodies obvious. Accordingly, Applicants respectfully request that this rejection be withdrawn.

The rejection of claims 75, 79, 81, 83 and 93 under 35 U.S.C. § 103 as allegedly obvious over Nagai et al., *supra*, in view of Campbell, *supra*, and further in view of Paul, Fundamental Immunology pp. 460-461, Raven Press, New York (1993), is respectfully traversed. Applicants respectfully submit that the claims are unobvious over Nagai et al., alone or in combination with Campbell and/or Paul.

As discussed above, Nagai et al. does not teach or suggest the specifically recited sequence referenced as SEQ ID NO:24. Accordingly, Nagai et al., alone or in combination with Campbell and/or Paul, does not teach every element of the claimed antibodies. Absent such a teaching or suggestion, Nagai et al., alone or in combination with Campbell and/or Paul, cannot render the claimed antibodies obvious. Accordingly, Applicants respectfully request that this rejection be withdrawn.

In light of the amendments and remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to call the undersigned agent if there are any questions.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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